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### STATE-OF-THE-ART PAPER



### CLINICAL RESEARCH

### STATE-OF-THE-ART PAPER

#### Oxidative Stress and Pathological Changes After Coronary Artery Interventions 1471

Rio P. Juni, Henricus J. Duckers, Paul M. Vanhoutte, Renu Virmani, An L. Moens

Coronary interventions are associated with increased vascular levels of reactive oxygen species (ROS) in conjunction with altered function of endothelial and smooth muscle cells. These alterations potentially lead to restenosis, thrombosis, or endothelial dysfunction in the peristent segment. This review discusses the molecular mechanisms of ROS generation after coronary interventions, the related pathological events, including restenosis, endothelial dysfunction, and stent thrombosis, and possible therapeutic ways forward. Current innovations, including biodegradable stents, nitric oxide donor-coated stents, and a new generation of drug-eluting stents, are proposed to address the persistent oxidative stress and reduced nitric oxide bioavailability after percutaneous coronary interventions.

### INTERVENTIONAL CARDIOLOGY

#### Double Kissing Bailloon Superior to Culotte Stenting for Distal Left Main Lesions 1482

Shao-Liang Chen, Bo Xu, Ya-Ling Han, Imad Sheiban, Jun-Jie Zhang, Fei Ye, Tak W. Kwan, Chittrapai Paiboon, Yu-Jie Zhou, Shu-Zheng Lv, George D. Dangas, Ya-Wei Xu, Shang-Yu Wen, Lang Hong, Rui-Yan Zhang, Hai-Chang Wang, Tie-Ming Jiang, Yan Wang, Fang Chen, Zu-Yi Yuan, Wei-Min Li, Martin B. Leon

The DKCRUSH-III study randomized subjects with unprotected left main coronary artery distal bifurcation lesions to either double kissing (DK) crush or Culotte stenting techniques. A total of 419 patients were randomly assigned with a primary endpoint of major adverse cardiac event (MACE) at 1 year. The MACE rate was significantly higher in the Culotte group, mainly driven by increased target vessel revascularization. In-stent restenosis rate in side branch was 12.6% in the Culotte group and 6.8% in the DK group. These results suggest that DK should be the preferred option for left main bifurcation lesions.

## VALVE DISEASE

## Outcome of Combined Stenotic and Regurgitant Aortic Valve Disease

1489

Robert Zilberszac, Harald Gabriel, Michael Schemper, David Zahler, Martin Czerny, Gerald Maurer, Raphael Rosenbek

The combination of aortic stenosis (AS) and aortic regurgitation (AR) may increase transvalvular flow interfering with echocardiographic indices of valve function and thus prognosis. Zilberszac and colleagues reviewed records from 71 consecutive asymptomatic patients with at least moderate AS in combination with at least moderate AR and preserved left ventricular function. There were no cardiac deaths during 9 years of follow-up. One-half of patients with a peak aortic jet velocity (AV-Vel) between 3 and 3.9 m/s at baseline had surgery AVR surgery by 6 years, compared to all patients with an AV-Vel  $\geq 5$  m/s. These results imply that AV-Vel, which reflects both stenosis and regurgitant severity, provides an objective and easily assessable predictive parameter.

*Editorial Comment: Benjamin Byrd, Michael Baker, p. 1496*

## HEART FAILURE

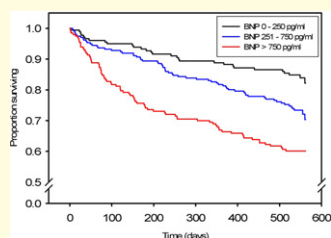
## BNP Predicts Mortality Better Than LVEF for Patients With HF

1498

Dirk J. van Veldhuisen, Gerard C. M. Linssen, Tiny Jaarsma, Wiek H. van Gilst, Arno W. Hoes, Jan G. P. Tijssen, Walter J. Paulus, Adriaan A. Voors, Hans L. Hillege

van Veldhuisen and colleagues sought to determine the prognostic value of brain natriuretic peptide (BNP) in patients with heart failure with preserved ejection fraction (HFPEF), in comparison to heart failure patients with reduced left ventricular ejection fraction (HFREF). Over 600 patients who had been hospitalized for heart failure (HF) were followed. BNP levels were significantly higher in patients with reduced ( $<40\%$ ) left ventricular ejection fraction (LVEF). BNP was a strong predictor of outcomes, but ejection fraction was not. For similar levels of BNP, the prognosis was equivalent for HFPEF patients and those with HFREF. These results suggest that BNP offers robust and similar prognostic information for patients with congestive HF regardless of the LVEF.

*Editorial Comment: James L. Januzzi, Jr., p. 1507*



## HEART FAILURE

## Lifetime Risk for Developing HF

1510

Mark D. Huffman, Jarrett D. Berry, Hongyan Ning, Alan R. Dyer, Daniel B. Garside, Xuan Cai, Martha L. Daviglus, Donald M. Lloyd-Jones

Huffman and colleagues noticed that prior estimates of lifetime risk for developing heart failure (HF) did not include sufficient numbers of black patients. Data was combined from 3 large cohort studies to estimate the lifetime risks for developing HF, with death free of HF as the competing event. At age 45 years, lifetime risks for HF through age 95 years were 30% to 42% in white men, 20% to 29% in black men, 32% to 39% in white women, and 24% to 46% in black women. The authors noticed higher competing mortality risks from other diseases or accidents may have lowered the risk in black men. These are among the first data to compare lifetime risks for HF between blacks and whites.

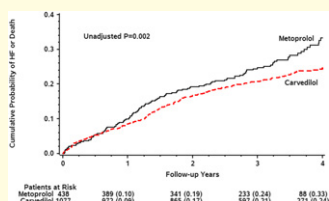
## HEART FAILURE

## Carvedilol Associated With Improved Outcomes Compared to Metoprolol in the MADIT-CRT Patients

1518

Martin H. Ruwald, Anne-Christine H. Ruwald, Christian Jons, Jeffrey Alexis, Scott McNitt, Wojciech Zareba, Arthur J. Moss

Ruwald and colleagues reviewed data from all patients receiving either metoprolol or carvedilol in the MADIT-CRT study, which randomized New York Heart Association functional class I to II patients with standard implantable cardioverter-defibrillators (ICD) indications, to either ICD or cardiac resynchronization therapy (CRT). Treatment with carvedilol was associated with a significantly decreased risk of hospitalization for heart failure or death when compared to metoprolol (hazard ratio [HR]: 0.70). This reduction in risk was further attenuated in the subgroup of CRT-D patients (HR: 0.62) and CRT-D patients with left bundle branch block (HR: 0.51). Although this was not a randomized trial, the results strongly suggest that carvedilol offers more benefits for these types of patients than metoprolol does.



## HEART RHYTHM DISORDERS

## Use of ICDs in Children and Adolescents With HCM

1527

Barry J. Maron, Paolo Spirito, Michael J. Ackerman, Susan A. Casey, Christopher Semsarian, N. A. Mark Estes III, Kevin M. Shannon, Euan A. Ashley, Sharlene M. Day, Giuseppe Pacileo, Francesco Formisano, Emmanuela Devoto, Aristidis Anastasakis, J. Martijn Bos, Anna Woo, Camillo Autore, Robert H. Pass, Giuseppe Boriani, Ross F. Garberich, Adrian K. Almquist, Mark W. Russell, Luca Boni, Stuart Berger, Martin S. Maron, Mark S. Link

Hypertrophic cardiomyopathy (HCM) is the most common cause of sudden death (SD) in the young, but there are limited data on the use of implantable cardioverter-defibrillators (ICDs) in children and adolescents. Maron and colleagues reviewed a multicenter international registry of ICDs implanted in 224 children and adolescents with HCM. Defibrillators activated appropriately to terminate ventricular tachycardia/fibrillation in 19% of patients, with an appropriate ICD intervention rate of 14%/year for secondary prevention and 3.1% for primary prevention. ICD-related complications, particularly inappropriate shocks and lead malfunction, occurred in 41% of patients. These results confirm the utility of, and the risks of, ICDs for children and adolescents with HCM.

*Editorial Comment: Mark V. Sherrid, p. 1536*

## CARDIAC IMAGING

CMR Shows Reduced LV and RV Function But No Fibrosis  
After Anthracycline Treatment for Childhood Cancer

1539

Kaisa Ylänen, Tuija Poutanen, Päivi Savikurki-Heikkilä, Irina Rinta-Kiikka, Anneli Eerola, Kim Vetterranta

The pathogenesis of late-onset cardiac toxicity of anthracyclines remains incompletely understood, but evidence suggests myocyte apoptosis which should produce myocardial fibrosis. This fibrosis would be detectable as late gadolinium enhancement (LGE) on cardiac magnetic resonance (CMR) imaging. Ylänen and colleagues studied 62 anthracycline-exposed long-term survivors of childhood cancer with CMR approximately 10 years after their exposure. A left ventricular (LV) ejection fraction (EF) <45% was detected in 18%, and a further 61% had an EF <55%, but >45%. Similar rates were seen for right ventricular (RV) function. Both the LV and RV end-systolic and LV end-diastolic volumes were increased compared to reference values. None of the study patients showed LGE. These results show high rates of reduced RV and LV function after anthracycline exposure without LGE.